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I was asked to find a way to further solubilize CoQ10 than the ~5% that theoretically could be obtained in soybean oil, and to use some kind of cosolvent if needed. My first guess was to solubilize it in D-Limonene, because it acts like a total solvent with beeswax — you need $\geq 10\%$ beeswax in formulations that have a high limonene content because it just dissolves the beeswax like it wasn't there. So I took 50g of D-limonene and started stirring in CoQ10, one or two gphs at a time, by hand, and at room temperature. I stopped at 40% CoQ10 (20 grams in 50g D-limonene), although I could have dissolved more in there. After about 30%, or so, the solution starts to get a little cloudy after adding the CoQ10, but with 1-3 minutes of steady slow stirring at the gphs rate the CoQ10 completely dissolves and the solution clears up. After getting a clear, dark red, 40% solution of CoQ10 in D-limonene, I wanted to see what would happen when the solution was added to oil, since pure D-limonene isn't real practical for a softgel fill — although we do make such a product. I added the CoQ10/D-limonene solution to 50g of soybean oil — 1 or 2 g at a time — until I ended up adding the entire amount of CoQ10 solution to the soybean oil. It resulted in a clear, dark red solution, with no precipitation or phase separation at all — we'll see how it is after some time passes, although I don't expect anything bad to occur at all. The final soybean oil/D-limonene/CoQ10 overall is 20% of CoQ10 that is completely solubilized.

3/17

The 20% CoQ10 in 50:50 SBO/Limonene shows ~1-2% precipitation out over the weekend (~51gives).

The trial that I added 10% a-lipoic acid shows the same amount of ? powder at the bottom as on Friday, which is mostly or all a-lipoic acid.

The one w/ 10% glycerin S+H has the glycerin at the bottom, separated, but no other precipitate is visible.

The one w/ 10% vitamin E solubilized nicely (amber-brown) when I first added it, which it still is, before precipitation.

The one I added 10% water to precipitated a very small amount at the interface.

The one w/ 10% licorice shows no separation or precipitation.

Next I am going to try and make a solubilized CoQ10 in lithophane softgels and then finally make some CoQ10 emulsions, with and To Page No. 145

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			3/14/00
		Received by	

TITLE Solubility of CoQ10 (Cont'd)

Project No. 202

Book No. 2

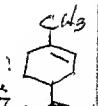
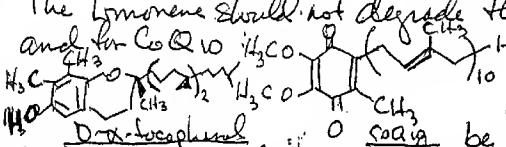
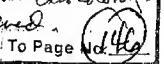
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From Page No. 144 Any beeswax and see how it comes out and how it behaves after some time passes. The formula for Co-Q10 (Colloid 100 mg) is:

		100 grams:
Co-PA-MX-00016	Cocoxyleno Q10	104.0900 mg
V.I.FA-MX-00191	4-SO MeTocopherol 372:20%	269.0300 mg
PIFF-MK-00077	Rice Bran Oil	176.0200 g.
BE-PA-MX-00053	Yellow Beeswax	20.0000 g.
BE-FA-MX-00203	Natural Beta-Carotene 255,500%	10.0000 g.
		<u>380.0000 g.</u>

I'm going to try, first of all, to remove the Beeswax and the Rice Bran Oil and dissolving the CoQ10 in the same amount of Limonene that would be the weight of the RBO and beeswax together (196.0200 mg/kg). So there'll be enough to dissolve it, then add the Vitamin E & Beta-Carotene. Hopefully, the Vitamin E will help to keep the CoQ10 dissolved. See the trial in the small way I did on Friday — maybe I'll keep the Beta-Carotene out of the formula so I can see it for a few days — then add it. Anyway here is the formula I will use:

	100 grams:
Cocoxyleno Q10	104.0900 mg
4-SO MeTocopherol	269.0300 mg
D-Limonene	196.0200 mg
Natural Beta-Carotene	10.0000 g.
	<u>580.0000 g.</u>

The Limonene should not degrade the CoQ10 as the formula for Limonene is:  and for CoQ10 it is:  — there is nothing there that will react with ether, so there should be no problem — the Limonene is just acting as an organic solvent — nothing more, nothing less. Wow! As soon as you add the Vitamin E to it (and it's very light-colored Vitamin E) it turns a dark purple color! I hope it's just due to a change in oxidation state of one or both the Vitamin E and CoQ10 — there isn't anything that should react to change the structure of anything there. Well since CoQ10 is the same amt as VTE in the other one — no decoloring. So I will go back to the lab and do some assays done to see if anything happened. 

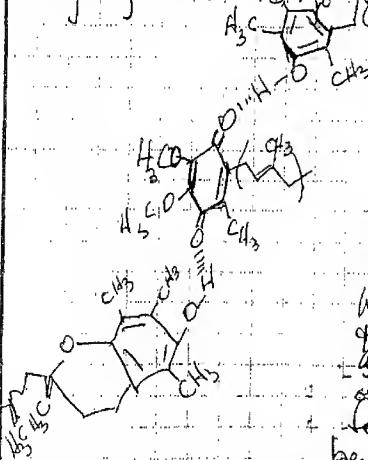
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(146) happened? The fully oxidized ketone groups on the glucose moiety of the CoQ₁₀ oxidized the hydroxyl group of the Chromenol on the D-a-Torophenol becoming a semi-quinone — Since the CoQ₁₀ is fully solubilized and the two molecules are in a compatible solvent, this would happen easily. There is nothing in any of the three molecules that could do anything else (no bonds broken, no additions/breakdowns/allisomerization happening or anything) — there has not been a change in the oxidation state and the solution absorbs light at a different wavelength, that's all — in fact, it would make both molecules more like their active states, anyway. A similar thing happens to the Shikle CoQ₁₀ product in the slot — it changes from an orange color to a dark brick red as the CoQ₁₀ becomes more solubilized and reacts with the Vitamin E in the product. It doesn't get as dark as the Shikle 1) there isn't as much Vitamin E in the Shikle product and 2) the CoQ₁₀ doesn't solubilize as much in the Shikle product — both things happen here, and all the constituents are just as active as they should be.

The mixture that I made last night with less than a half gram of the Vitamin E looked real good last night, but was very precipitated today — no good. I'm really encouraged with this project though.

Thinking more on the interaction between the CoQ₁₀ and Vitamin E, it may only be due to hydrogen bonding between the molecules, like this:



Even if the two molecules were, in fact, causing partial oxidation state changes in each other, or if they were hydrogen bonding either one is fine as far as their function and activity goes, and the only real change in them is not structural, or binding, so I don't see any problem here, other than maybe having to convince some of the less technical ones here about what, in fact, is happening and that the color change is nothing to worry about — actually, if they are ever changing the oxidation state of each other, this is often toward the more functional form of both molecules. I can only help — I'd be enormously surprised if it were anything else.

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			3/18/03

Recorded by

TITLE Colo Solubility

From Page No. 146 When I added DL-tocopherol acetate to the solubilized ColQ₁₀/Limonene there was no decoloration - it stayed the clear pale color. But after sitting overnight there is a slight amount of precipitation on the bottom of the vial. There is also a slight amount of precipitation on the bottom of the vial & beaker with the D-alpha-tocopherol and the DL-tocopherol acetate beaker - 33% ColQ₁₀ appears to be too concentrated - I'll have to bring it down to 30% or 28% and see how that does.

3/21/03

It's evident that the limonene is evaporating out of the open beakers, and that may be one of the reasons that I'm getting precipitation - although it is just a small amount (~1-2%). Here's an interesting note from the beaker that showed some precipitation after a day of sitting out last night more limonene remained on the second night, but the small amount of precipitation that formed the day before re-solubiled spontaneously. The only thing that I can think of that may be causing this is that over the 48 hours or so that the ColQ₁₀ was in the (vial), it needed that much time for a small amount of limonene to completely solubilize an even larger amount of ColQ₁₀. It sounds a bit confusing, but I can't think of any other reason for this happening.

As for the assay I requested on the mix I made that was comparable to our CC-930 100% ColQ₁₀, ~~it~~ it came out well - the ColQ₁₀ was 110% of claim and the Vitamin E (mixed tocopherols) came out with good results for the separate corners; in fact the Gamma-tocopherol peak was as high as the D-alpha-peak for our Chem 4-50 Vitamin E. There were no unexpected peaks in either assay, so it proves my claim that the limonene doesn't hurt any of the substances and that the color change that occurs after adding the vitamin E to the solubilized ColQ₁₀ is not due to anything other than a change in oxidation state. I'm very encouraged by all this, and am starting to hear exactly what they want me to do with it - there's a lot of possibilities here, if we do it right.

3/26/03

Now I'm told to go ahead and try solubilizing 28-30% ColQ₁₀ in limonene but they want me to add sorbic acid or something to it - just don't like the idea of so much money getting thrown away. I won't hesitate trying the mix I made up before - off the 100% ColQ₁₀ product - the one that tested out so well, ended up with a small amount of crystals that formed on the bottom of the vial over time, so I'm convinced that ~33% B is just too much for it - but adding all that much

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With amine E - or anything else increases the chance that the Colloids will precipitate out. The one with 33% Colloids in it from me and only 10% amine added, back on 3/14 still shows no precipitation, so that's encouraging, but I really don't think we need to add anything else. Just the Colloids in themselves the amine was + hurt 1200 ppm, and it's already grand tailored in as a safe nutritional supplement ingredient, so there's no regulatory problems with it.

(End)

From Page No. 1

Sample of:
Here is the

AS-FA-MX-1
VI-FA-MX-1
VI-FA-MX-0
VB-FA-MX-1
VB-FA-MX-0
NI-FA-MX-1
NI-FAMX-1
VB-FAMX-1
FO-FA-MX-1
VBFA-MX-1
BI-FA-MX-
CA-FA-MX-
PA-FA-MK-
LI-FA-MX-
SE-FA-MX-1
CH-FA-MK-
IN-FA-MX-1
HO-FA-MX-
CO-FA-MX-1
SA-PA-SK-
PU-FF-MK-
AV-FA-MX-
MA-FA-MX-1
LE-FA-MX-
BE-PA-MX-
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3/16/63